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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/785,559	02/16/2001	Karl-Heinz Boven	WITTE-011XX	3534

207 7590 07/30/2003

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EXAMINER

BEISNER, WILLIAM H

ART UNIT PAPER NUMBER

1744

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/785,559

Applicant(s)

BOVEN ET AL.

Examiner

William H. Beisner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15, 17-26 and 30-58 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 57 is/are allowed.
- 6) ☒ Claim(s) 1-15, 17-26, 30-38, 40-44, 46-56 and 58 is/are rejected.
- 7) ☒ Claim(s) 39 and 45 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The indicated allowability of claims is withdrawn in view of the newly discovered reference(s) to Lee et al. Rejections based on the newly cited reference(s) follow.

Claim Objections

2. Claims 21, 22, 23 and 25 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 from which claim 21 depends recites that the electrode is a measuring electrode. Claim 21 recites that the electrode is a reference electrode. As a result, claim 21 does not include all of the limitations of the claim from which it depends. As currently written, claim 21 does not include a measurement electrode.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 2, 7, 10, 11, 31, 37, 38, 40, 55 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al.(US 4,128,456).

With respect to claim 1, the reference of Lee et al. discloses a device that includes a measuring head (8) provided with at least one measuring electrode (28) for impaling cells (60). The measuring head (8) also includes at least one perfusion conduit (36) made as a perfusion inlet having a first end opening, wherein the at least one measuring electrode (28) is integrated into a support (29) and the electrode (28) and perfusion conduit (36) are arranged essentially parallel with respect to one another. Finally, the opening of the perfusion conduit (36) is located above a lower end of the electrode (28).

With respect to claim 2, electrode (28) is inserted into recess (26).

With respect to claim 7, electrode (28) is disclosed as a wire electrode (See column 3, lines 43-47).

With respect to claim 10, the electrode (28) has a straight section as shown in the drawings.

With respect to claim 11, electrode (28) includes an end or tip that is capable of penetrating a cell.

With respect to claim 31, the perfusion inlet is fluidly connected to pump (51).

With respect to claims 37, 38, 55 and 58, the device include perfusion outlet conduit/opening (48/50) wherein opening (50) is above to opening of conduit (36). Note the perfusion inlet, outlet and electrode are all supported on measuring head (8).

With respect to claim 40, the perfusion outlet is connected to pump (51).

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5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 3, 32 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 4,128,456).

The reference of Lee et al. has been discussed above.

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With respect to claim 3, while the reference discloses that electrode (28) is removable from the measuring head, it would have been obvious to one of ordinary skill in the art to construct the electrode as an integral part of the head for the known and expected result of providing an alternative means recognized in the art for providing the unitary device. For example, the unitary device may be disposable and there would not be a need to have electrode (28) be removable from the rest of the device.

With respect to claims 32 and 41, while the reference of Lee et al. does not specifically recite that pump (51) is adjustable, it would have been obvious to provide a pump that is adjustable for the known and expected result of providing a means recognized in the art for controlling the suction and/or flow of perfusion fluid within the perfusion chamber.

9. Claims 4-6, 8, 9, 12-14, 17-26, 30, 33-36, 42, 43, 46, 49, 52, 54 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 4,128,456) in view of Olesen et al.(WO 98/50791).

The reference of Lee et al. has been discussed above.

With respect to claims 4-6, 8 and 9, these claims differ by reciting the specifics of the electrode employed in the device.

The reference of Lee et al. discloses that two types of microelectrodes are known in the art, a fine wire (28) as disclosed by Lee et al. and a finely drawn glass tube (See column 1, lines 19-30).

The reference of Olesen et al. discloses an electrode system for measuring cell events in cells wherein the reference discloses the specifics of finely drawn glass tube electrodes (See page

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30) which discloses the use of a glass tube and silver-silver chloride electrode (63) and has a resistance of 2-6 M Ω .

In view of these teachings, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ an electrode configuration as disclosed by the reference of Olesen et al. in the system of the primary reference for the known and expected result of providing an alternative means recognized in the art to achieve the same result, measuring cell membrane events.

With respect to the use of plural electrodes as recited in claims 12, 13, 21-26, 30, 42, 54 and 56, while the reference of Olesen et al. depicts only one electrode mounted on a head as is also shown by the primary reference of Lee et al., the reference of Olesen et al. discloses that the head may optionally hold other electrodes for completing voltage and current loops (See page 23).

In view of this teaching and in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the device of the primary reference with additional electrodes (measuring, reference, etc.) as suggested by the reference of Olesen et al. for the known and expected result of completing voltage and current loops used in the detection system. With respect to the placement of the electrodes with respect to one another and referenced planes, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the plurality of electrodes relative to the support head while maintaining the electrodes in a position such that a single cell is capable of being penetrated by the required electrodes and/or electrodes are capable of contacting the perfusion fluid. Further note that electrodes that are parallel to one

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another meet the claim limitation that the electrodes are symmetrical and form an acute angle.

With respect to the claimed distance of the tips of the electrodes, it would have been obvious to determine the optimum spacing of plural electrodes based merely on the size of the cell to be penetrated while maintaining a configuration that allows the cell to be penetrated by plural electrodes.

With respect to claims 17-20, while the reference of Lee et al. discloses control and recording device (66), the reference is silent as to the specifics of this configuration.

The reference of Olesen et al. discloses the electrical circuitry that is required to measure the cells (See page 23, lines 5-24).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ a current and voltage control system as disclosed by the reference of Olesen et al. in the system of the reference of Lee et al. for the known and expected result of providing a means recognized in the art for measuring cell potential.

With respect to claims 43, 46 and 49, while the reference of Lee et al. discloses a measuring head (8), the reference is silent as to the use of the head in combination with a movable actuator.

The reference of Olesen et al. discloses that it is known in the art to mount the electrodes of an electrophysiological measuring device on a micromanipulator device (see page 23). The reference discloses that the micromanipulator can support a plurality of electrodes. The reference also discloses patch clamp electrodes with a resistance of 2-5Mohms (See page 30).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to mount the electrodes of the primary reference of a

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micromanipulator as suggested by the reference of Olesen et al. for the known and expected result of providing a means recognized in the art for automating the positioning of the electrodes relative to the cells to be impaled for detection. With respect to the manner in which the electrode is attached to the micromanipulator would have been merely an obvious matter in design choice based on considerations. The use of microtiter plates for supporting the cells would have been obvious since their use in automated device is well known in the art in view of the 96 well standard in which the automated devices are manufactured and programmed.

With respect to the use of pumps and solution reservoirs (see claims 33-36), the reference of Olesen et al. discloses (See Figure 1) a perfusion system which is known and would have been obvious for the known and expected result of testing the cells to different types of chemical stimulations.

10. Claims 15 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 4,128,456) in view of Olesen et al.(WO 98/50791) and Takeshita et al.(US 6,277,559).

The combination of Lee et al. and Olesen et al. has been discussed above.

The above claims differ by reciting that the acute angle formed by the electrode pairs is between 3-10, preferably 5, degrees.

The reference of Takeshita et al. discloses that it is known in the art to penetrate the cell with electrodes that are at an angle relative to vertical (See the figures).

In view of this teaching, it would have been obvious to one of ordinary skill in the art when employing plural electrodes, to mount the electrodes at an angle relative to vertical for the known and expected result of providing a means recognized in the art for allowing a plurality of

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electrodes to penetrate a single cell. With respect to the specific angle employed, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to determine the optimum angle of the electrodes while providing a reliable means for impaling the cells to be measured.

11. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 4,128,456) in view of Olesen et al.(WO 98/50791) and Byrne et al.(WO 00/34776).

The combination of the references of Lee et al. and Olesen et al. has been discussed above.

While the references disclose mounting the electrodes on a micromanipulator, the references do not disclose the use of a plurality of measuring heads on a single manipulator.

The reference of Byrne et al. discloses that it is known in the art to provide a plurality of measuring electrodes on a single carrier while measuring a plurality of cells in a plurality of difference measuring chambers (See Figure 24).

In view of this teaching, which using a plurality of cell chambers or wells, it would have been obvious to one of ordinary skill in the art to provide a single micromanipulator which carries a plurality of detection electrode sets for the known and expected result of allowing a plurality of cells to be measured simultaneously and be simultaneously impaled using a single manipulator.

12. Claim 47 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 4,128,456) in view of Olesen et al.(WO 98/50791) and Farb et al.(US 6,048,722).

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The combination of the references of Lee et al. and Olesen et al. has been discussed above.

The claims further require that the carrier includes a cell injection device.

The reference of Farb et al. discloses that it is known in the art to provide electrophysiological measurement device with cell injection devices (See column 3, lines 15-24).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to include a microinjection needle in the manipulator device for the known and expected result of providing a means recognized in the art for injecting nucleic acids into the cells as is suggested by the reference of Farb et al.

13. Claims 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 4,128,456) in view of Olesen et al.(WO 98/50791) and Carr et al.(US 5,888,825).

The combination of the references of Lee et al. and Olesen et al. has been discussed above.

The claims differ by reciting that individual cell receptacles within the device are identified by bar codes and the manipulator includes a bar code reader.

The reference of Carr et al. discloses that it is well known in the art when monitoring a plurality of reaction vessels to identify each receptacle using bar codes and to use a bar code reader on the device monitoring the reaction in each vessel (See column 4, line 65 to column 5, line 5).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the micromanipulator with a bar code reader for identifying a selected reaction chamber

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when performing a plurality of tests as is disclosed in the reference of Olesen et al. (See Figures 13 and 16).

Allowable Subject Matter

14. Claim 57 is allowed.

15. Claims 39 and 45 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. The following is a statement of reasons for the indication of allowable subject matter:

With respect to claims 57 and 45, while the prior art of record suggest the use of an actuator for mounting a plurality of electrode heads, the prior art of record fails to teach or fairly suggest that the measuring heads are adapted to be displaced individually relative to said actuator along an axis z directed toward the cells.

With respect to claim 39, while the prior art of record suggests the combination of a perfusion inlet, perfusion outlet and measuring electrode all mounted on the same measuring head, the prior art of record fails to teach or fairly suggest a configuration wherein the ends of the perfusion inlet and outlet are oriented in opposite directions.

Response to Arguments

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17. Applicant's arguments, see page 14, line 14, to page 15, line 9, filed 20 May 2003, with respect to the rejection(s) of claim(s) 1-28, 31-37, 40, 41, 43, 44 and 46-53 under various combinations of the cited prior art have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Lee et al. (US 4,128,456).

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 703-308-4006. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:40am to 4:10pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 703-308-2920. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9310 for regular communications and 703-872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.


William H. Beisner
Primary Examiner
Art Unit 1744

WHB
July 26, 2003